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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,866	05/29/2001	Brian Sorrentino	02427/1203347-US2	4688

29311 7590 06/02/2009

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ART UNIT	**PAPER NUMBER**
1644	

MAIL DATE	DELIVERY MODE
06/02/2009	PAPER

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte BRIAN SORRENTINO and JOHN SCHUETZ

Appeal 2009-000923
Application 09/866,866
Technology Center 1600

Decided[1]: June 2, 2009

Before TONI R. SCHEINER, DONALD E. ADAMS, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to an antibody to a Breast Cancer Resistance Protein (BCRP). We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, begins to run from the decided date shown on this page of the decision. The time period does not run from the Mail Date (paper delivery) or Notification Date (electronic delivery).

Statement of the Case

Background

"[T]he BCRP [Breast Cancer Resistance Protein] gene is expressed at relatively high levels both in primitive CD34-murine HSCs [human stem cells] and in SP [side population] cells from the bone marrow" (Spec. 11, ll. 9-11). The Specification notes that "[c]ell sorting for BCRP expression using appropriate antibodies provides a new strategy for stem cell purification applicable to cells from different organ sources" (Spec. 12, ll. 30-32).

The Claims

Claims 16, 22-24, and 29-34 are on appeal. We will focus on independent claim 16, which is representative and reads as follows:

> 16. An isolated antibody that binds to an extracellular portion of a Breast Cancer Resistance Protein (BCRP) selected from the group consisting of human BCRP_(huBCRP) or murine BCRP (mBCRP); wherein the extracellular portion of the BCRP is in its natural conformation; wherein the antibody binds to living MCF-7 or 3T3 cells expressing BCRP on their surface; wherein the antibody does not bind to living MCF-7 cells that do not express BCRP on their surface; and wherein the antibody does not bind to denatured BCRP.

The prior art

The Examiner relies on the following prior art references to show unpatentability:

Zuk	US 4,281,061	Jul. 28, 1981
Ross	US 6,313,277 B1	Nov. 6, 2001
Bandman	US 6,485,933 B1	Nov. 26, 2002

Owens et al., *The genetic engineering of monoclonal antibodies*, 168 J. IMMUNOLOGICAL METHODS 149-165 (1994).

Appellants rely on the following additional evidence

Sarkadi Declaration, October 27, 2003.
Sarkadi Declaration, January 17, 2005

The issues

A. The Examiner rejected claims 16, 22-24 and 29-34 under 35 U.S.C. § 112, second paragraph as being indefinite (Ans. 4).

B. The Examiner rejected claims 16, 22 and 31-34 under 35 U.S.C. § 102(e) as being anticipated by Ross (Ans. 4-5).

C. The Examiner rejected claims 16, 22-24 and 29-34 under 35 U.S.C. § 102(e) as being anticipated by Bandman (Ans. 5-6).

D. The Examiner rejected claims 16, 23, 24, and 29 under 35 U.S.C. § 103(a) as being obvious over Ross and Owens (Ans. 6-7).

E. The Examiner rejected claims 16 and 30 under 35 U.S.C. § 103(a) as being obvious over either Ross or Bandman in view of Zuk (Ans. 8).

A. 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 16, 22-24 and 29-34 under 35 U.S.C. § 112, second paragraph as being indefinite (Ans. 4).

The Examiner finds that "[r]ecitation of a protein without providing SEQ ID NO for the protein is indefinite and ambiguous because different laboratories may have the same name for a different protein" (Ans. 4).

Appellants contend that "[t]he terms 'huBCRP' and 'mBCRP' are not indefinite because, reading the specification, one of ordinary skill in the art knows that these terms correspond to a set of well-defined proteins,

identified by SEQ ID in the specification. There is no ambiguity in what is claimed by using the terms huBCRP and mBCRP" (App. Br. 5).

In view of these conflicting positions, we frame the definiteness issue before us as follows:

Did the Examiner err in finding that the claims are indefinite based upon the recitation of BCRP without a sequence identification number?

Findings of Fact (FF)

1. Claim 16 recites BCRP and specifically limits the BCRP to antibodies against the human and murine BCRP extracellular regions (*see* Claim 16).

2. The Specification teaches that "[n]ames in the literature of genes encoding this protein include *Bcrp1*, *Mxr*, *Abcp* and ABCG2 gene" (Spec. 15, ll. 3-4).

3. The Specification teaches that "'BCRP' is meant to include all of such ATP transport proteins obtained from any mammalian source. The murine protein is also referred to herein as mBCRP, whereas the human protein is termed herein, 'huBCRP'" (Spec. 15, ll. 6-8).

4. The Specification teaches two different nucleic acid and amino acid sequences for both human and murine BCRP (*see* Spec. 15, ll. 10-16).

Principles of Law

"The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification." *Miles Laboratories, Inc. v. Shandon, Inc.*, 997 F.2d 870, 875 (Fed. Cir. 1993).

Claims are in compliance with 35 U.S.C. § 112, second paragraph, if "the claims, read in light of the specification, reasonably apprise those skilled in the art and are as precise as the subject matter permits." *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385 (Fed. Cir. 1987).

> Although "it is entirely proper to use the specification to interpret what the patentee meant by a word or phrase in the claim, ... this is not to be confused with adding an extraneous limitation appearing in the specification, which is improper. By 'extraneous,' we mean a limitation read into a claim from the specification wholly apart from any need to interpret ... particular words or phrases in the claim." *E.I. du Pont de Nemours & Co. v. Phillips Petroleum Co.*, 849 F.2d 1430, 1433, 7 USPQ2d 1129, 1131 (Fed. Cir.), cert. denied, 488 U.S. 986, 109 S. Ct. 542, 102 L.Ed.2d 572 (1988).

In re Paulsen, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Analysis

The Examiner fails to explain why simply because multiple laboratories may have different names for a protein or nucleic acid, the use of one of those names is indefinite. In this case we are not looking to the Specification to add an extraneous limitation to the claim; instead, we look to the Specification to ascertain the meaning of the claim term BCRP as it is used by the inventor in the context of the entirety of his invention (FF 1-4).

The Specification recognizes multiple names for BCRP, and harmonizes those different names under the rubric of BCRP (FF 2). The Specification also clearly defines BCRP, and in particular, defines the human and murine BCRP molecules (FF 3). This definition clearly excludes other random proteins which are not ATP transporters from falling within the scope of the claim (FF 3). The Specification provides two exemplary

sequences each for the human and murine BCRP (FF 4). "[I]t is entirely proper to use the specification to interpret what the patentee meant by a word or phrase in the claim." *In re Paulsen*, 30 F.3d at 1480.

Conclusion of Law

The Examiner erred in finding that the claims are indefinite based upon the recitation of BCRP without a sequence identification number.

We reverse the rejection of claims 16, 22-24 and 29-34 under 35 U.S.C. § 112, second paragraph as being indefinite.

B. 35 U.S.C. § 102(e) over Ross

The Examiner rejected claims 16, 22 and 31-34 under 35 U.S.C. § 102(e) as being anticipated by Ross (Ans. 4-5).

The Examiner finds that Ross "teaches an isolated polyclonal and monoclonal antibody that binds to BCRP" (Ans. 4). The Examiner finds that "[a]lthough the reference is silent about the antibody binding to an extracellular portion of BCRP or does not bind to denatured BCRP, said functional limitation would be inherent properties of the referenced antibody, because the referenced antibody was obtained against the same antigen as claimed" (Ans. 4).

Appellants contend that "the '277 patent does not, in fact, disclose the *actual generation* of any antibody, let alone one that would necessarily bind to an extracellular portion of BCRP and *not* to denatured BCRP" (App. Br. 10). Appellants contend that "[t]his omission in the '277 patent is significant because there is nothing within the '277 patent from which one skilled in the art could deduce to what portion (if any) of BCRP the disclosed antibody would bind" (App. Br. 10).

In view of these conflicting positions, we frame the anticipation issue before us as follows:

Did the Examiner err in finding that antibodies to BCRP generated according to the disclosure of Ross would inherently bind "to an extracellular portion of a Breast Cancer Resistance Protein" where "the extracellular portion of the BCRP is in its natural conformation"?

Findings of Fact

5. The Specification teaches that "[t]he strategy of using living cells transduced with the vector increases the probability that the immune system will detect external huBCRP epitopes in their native configuration, rather than epitopes that are internally located in the cells, or epitopes only present in denatured protein" (Spec. 23, ll. 13-16).

6. Ross teaches that a "polyclonal antibody capable of binding to BCRP can be prepared by immunizing a mammal with a preparation of BCRP or functional derivative of BCRP. Methods for accomplishing such immunizations are well known in the art" (Ross, col. 4, ll. 50-54).

7. Ross teaches that "[m]onoclonal antibodies or fragments thereof can also be employed to assay for the presence or amount or BCRP in a particular biological sample. Such antibodies can be produced by immunizing splenocytes with activated BCRP" (Ross, col. 4, ll. 54-57).

8. Dr. Sarkadi states that "I have used an antibody produced in accordance with the method of U.S. Patent Application Serial No. 09/866,866 (*i.e.,* 5D3) and shown that the interaction of 5D3 with BCRP in intact cells is dependent upon the actual conformation within the transport cycle of this multidrug resistance protein" (Sarkadi Dec. 2/22/05 ¶ 7).

9. Dr. Sarkadi states that "an antibody generated against an N-terminal intracellular epitope of BCRP (*i.e.,* BXP-21) cannot recognize BCRP in a living cell. Therefore, this method is essential to producing an antibody which recognizes an extracellular portion of BCRP in its natural conformation" (Sarkadi Dec. 2/22/05 ¶ 7).

Principles of Law

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Analysis of whether a claim is patentable over the prior art under 35 U.S.C. § 102 begins with a determination of the scope of the claim. We determine the scope of the claims in patent applications not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction in light of the specification as it would be interpreted by one of ordinary skill in the art. *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364 (Fed. Cir. 2004). The properly interpreted claim must then be compared with the prior art.

"If the prior art reference does not expressly set forth a particular element of the claim, that reference still may anticipate if that element is 'inherent' in its disclosure." *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999). "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *Id.* (*quoting Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991)) (internal quotation marks and citations omitted).

Analysis

Each of the independent claims requires not only an antibody which binds to an extracellular portion of a BRCP, but further requires that the antibody bind the natural conformation of the BCRP and not bind to denatured BCRP (*see* Claims 16, 31, 33).

While Ross reasonably teaches an antibody which binds to BCRP (FF 6-7), Ross provides no evidence to suggest that any of the BCRP antibodies made according to the disclosed method will necessarily bind to the natural conformation of BCRP and not bind denatured BCRP, as required by the claims.

Additionally, the Sarkadi Declaration (2/22/05) states, without evidentiary contradiction by the Examiner, that "interaction of 5D3 with BCRP in intact cells is dependent upon the actual conformation within the transport cycle of this multidrug resistance protein" (Sarkadi Dec. 2/22/05 ¶ 7; FF 8).

We do not disagree with the Examiner that synthesis of either polyclonal or monoclonal antibodies is routine, or that there would not be a reasonable expectation of obtaining BCRP antibodies using the BCRP protein. However, the claims do not require simply obtaining antibodies, the claims require particular specificities in the antibodies for the natural conformation and not a denatured conformation, specificities which may be possible, but "[i]nherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999).

Here, the Examiner has not even shown that antibodies to the natural conformation *may* result from the disclosure of Ross, much less that the prophetic suggestion to form antibodies in Ross would result in an antibody which "necessarily functions in accordance with, or includes, the claimed limitations." *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1349 (Fed. Cir. 2002).

We are not convinced by the Examiner's statement that "it was [] well known in the art that antibodies raised against purified membrane-associated proteins were used in flow-cytometry or to detect or target *in vivo* cells expressing said membrane-associated proteins" (Ans. 14). Not only does the Examiner present no evidence to support this statement, but even if true, it does not address the fundamental issue of whether antibodies raised against BCRP would *inherently* (that is necessarily function) to bind BCRP in the natural conformation and not in the denatured conformation. The antibodies used in flow cytometry might bind to both the natural and denatured conformations. The Examiner has provided no evidence to support this inherency.

We also are not persuaded by the Examiner's reliance upon Ross's suggestion that BCRP antibodies can be administered to reduce resistance to chemotherapeutic drugs (*see* Ans. 12). Ross never synthesizes an antibody to BCRP and this speculation by Ross, which represents unclaimed subject matter, does not demonstrate that BCRP antibodies would necessarily bind to BCRP in the natural conformation and not bind denatured BCRP.

Conclusion of Law

The Examiner erred in finding that antibodies to BCRP generated according to the disclosure of Ross would inherently bind "to an extracellular portion of a Breast Cancer Resistance Protein" where "the extracellular portion of the BCRP is in its natural conformation".

We reverse the rejection of claims 16, 22 and 31-34 under 35 U.S.C. § 102(e) as being anticipated by Ross.

C. 35 U.S.C. § 102(e) over Bandman

The Examiner rejected claims 16, 22-24 and 29-34 under 35 U.S.C. § 102(e) as being anticipated by Bandman (Ans. 5-6).

The Examiner finds that Bandman "teaches an isolated polyclonal and monoclonal antibody that binds to BCRP (see entire document, Abstract and column 16, lines 15-30 in particular). US Patent '933 further teaches that said antibody is chimeric or humanized or attached to detectable label (see overlapping columns 18 and 19)" (Ans. 5).

Appellants contend that "prophetic disclosure of purely hypothetical antibodies does not support the Examiner's assertion that antibodies disclosed in the '933 patent would necessarily 'bind[] to an extracellular portion of a Breast Cancer Resistance Protein (BCRP)' and/or 'not bind to denatured BCRP' as recited in the instant claims" (App. Br. 14).

In view of these conflicting positions, we frame the anticipation issue before us as follows:

Did the Examiner err in finding that antibodies to BCRP generated according to the disclosure of Bandman would inherently bind "to an

extracellular portion of a Breast Cancer Resistance Protein" where "the extracellular portion of the BCRP is in its natural conformation"?

Findings of Fact

10. Bandman teaches "[a]ntibodies to BCRP may be generated using methods that are well known in the art. Such antibodies may include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, Fab fragments, and fragments produced by a Fab expression library. Neutralizing antibodies, (i.e., those which inhibit dimer formation) are especially preferred for therapeutic use" (Bandman, col. 18, ll. 58-64).

11. Bandman teaches that a "variety of protocols for detecting and measuring the expression of BCRP, using either polyclonal or monoclonal antibodies specific for the protein are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence activated cell sorting (FACS)" (Bandman, col. 16, ll. 16-21).

12. Bandman teaches monoclonal antibodies to BCRP and chimeric monoclonal antibodies to BCRP (*see* Bandman, col. 19, ll. 22-45).

13. Bandman teaches that "[a]ntibodies may also be produced by inducing in vivo production in the lymphocyte population or by screening recombinant immunoglobulin libraries or panels of highly specific binding reagents as disclosed in the literature" (Bandman, col. 19, ll. 46-49).

Analysis

As discussed *supra*, each of the independent claims requires not only an antibody which binds to an extracellular portion of a BRCP, but further

requires that the antibody bind the natural conformation of the BCRP and not bind to denatured BCRP (*see* Claims 16, 31, 33).

While Bandman reasonably teaches an antibody which binds to BCRP (FF 10-13), Bandman provides no teaching to select antibodies which bind to the natural conformation of the BCRP. Bandman provides no evidence to suggest that any BCRP antibodies will necessarily bind to the natural conformation of BCRP and not bind denatured BCRP, as required by the claims.

As we discussed supra, the Examiner has not even shown that antibodies to the natural conformation *may* result from the disclosure of Bandman, much less that the prophetic suggestion to form antibodies in Bandman would result in an antibody which "necessarily functions in accordance with, or includes, the claimed limitations." *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1349 (Fed. Cir. 2002).

We are not persuaded by the Examiner's reliance on Bandman's suggestion that the antibody may be used in FACS analysis (*see* Ans. 12-13). Bandman never synthesizes an antibody to BCRP and this speculation by Bandman regarding FACS analysis with antibodies which do not yet exist does not demonstrate that BCRP antibodies would necessarily bind to BCRP in the natural conformation and not bind denatured BCRP.

Conclusion of Law

The Examiner erred in finding that antibodies to BCRP generated according to the disclosure of Bandman would inherently bind "to an

extracellular portion of a Breast Cancer Resistance Protein" where "the extracellular portion of the BCRP is in its natural conformation".

We reverse the rejection of claims 16, 22-24 and 29-34 under 35 U.S.C. § 102(e) as being anticipated by Bandman.

D. and E. - 35 U.S.C. § 103(a) rejections

The Examiner rejected claims 16, 23, 24, and 29 under 35 U.S.C. § 103(a) as being obvious over Ross and Owens (Ans. 6-7).

The Examiner rejected claims 16 and 30 under 35 U.S.C. § 103(a) as being obvious over either Ross or Bandman in view of Zuk (Ans. 8).

We reversed *supra* the rejection of claims 16, 23, 24, and 29 under 35 U.S.C. § 102(e) as unpatentable over Ross and the rejection of claims 16 and 30 under 35 U.S.C. § 102(e) as unpatentable over Bandman. The Examiner presents the same arguments regarding inherency for the rejection of claims 16, 23, 24, 29, and 30 under U.S.C. § 103(a). The Examiner does not provide evidence, suggestion, or reasoning to render obvious BCRP antibodies which bind to BCRP in the natural conformation but do not bind denatured BCRP. The additional Zuk and Owens references provide no guidance to suggest such antibodies.

We reverse the rejection of claims 16, 23, 24, and 29 under 35 U.S.C. § 103(a) as being obvious over Ross and Owens. We reverse the rejection of claims 16 and 30 under 35 U.S.C. § 103(a) as being obvious over either Ross or Bandman in view of Zuk.

SUMMARY

In summary, we reverse the rejection of claims 16, 22-24 and 29-34 under 35 U.S.C. § 112, second paragraph as being indefinite.

We reverse the rejection of claims 16, 22 and 31-34 under 35 U.S.C. § 102(e) as being anticipated by Ross.

We reverse the rejection of claims 16, 22-24 and 29-34 under 35 U.S.C. § 102(e) as being anticipated by Bandman.

We reverse the rejection of claims 16, 23, 24, and 29 under 35 U.S.C. § 103(a) as being obvious over Ross and Owens. We reverse the rejection of claims 16 and 30 under 35 U.S.C. § 103(a) as being obvious over either Ross or Bandman in view of Zuk.

REVERSED

Ssc:

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